Appln No.: 09/960,665
Amendment Dated: October 5, 2005
Reply to Office Action of July 12, 2005

REMARKS/ARGUMENTS

This is in response to the Office Action mailed July 12, 2005 for the above-captioned application. Reconsideration and further examination are respectfully requested.

Because of the confusion concerning the pending claims, Applicants have canceled claims 1-34, and replaced them with a new set of claims 35-66.

The Examiner rejected the previously pending claims as lacking enablement. With respect to claim 1 (now claim 35), the Examiner asserted that "determining the compound claimed would require synthesis of millions of compounds and testing each to determine whether the compounds fall within the scope of claim 1." Applicants do not understand what this argument has to do with enablement. Bearing in mind that Applicants are not responsible for enabling future inventions, the Examiner has not alleged that there would be any difficulty in making a chemical compound with two presently known HSP-90 binding moieties connected by a linker or with testing the compound to see if the moieties retained the ability to bind to HSP-90. Thus, this is not a basis for an enablement rejection.

Dependent composition claims 36-43 further define the HSP-90 binding moiety and the linker. Applicants submit that the Examiner must consider each of these claim individually and explain why the particular claim is not enabled.

The Examiner included original claim 12 (now claim 44) in the rejection for lack of enablement. Presumably this claim and the claims dependent thereon were rejected on the same basis as composition claims. The same arguments therefore apply.

With respect to claim 13 (now claim 53) the Examiner asserted that the specification does not provide enablement for cancer generally. Applicants point out that claims 54-62 are specific to cancers that are HER-positive and not to cancers generally, and that claims 63-66 recite specific types of cancer. Thus, none of these recite cancer "generally" and the Examiner's arguments are therefore not applicable to these claims. No explanation of the application of this argument to claims limited to specific cancers or claims limited to HER-positive cancers has been provided.

The Examiner has finally in this Official Action commented on the declaration and the exhibits A-H which are of record in this case. However, Applicants submit that the cursory comments on the evidence fail to consider the evidence in context of the present invention.

The basis for the Examiner's argument is largely that the Examiner is classing cancer therapy with perpetual motion machines and assumes in assessing enablement that it is inherently

unbelievable that a cancer therapy could work generally. Such may have been the case when *In re Buting*, 163 USPQ 689 (CCPA 1969), cited by the Examiner, was decided in 1969, but the art and the law have progressed since then. The notion of automatic unbelievability is no longer credited. Indeed, as the Board of Appeals noted in 1987 in *Ex parte Rubin*, 5 USPQ2d 1461, 1462 (POBAI 1987), "'contemporary knowledge in the art ' has far advanced since the days when the any statement of utility in treating cancer was per se 'incredible.'" Here, the Examiner has not offered any reasoning as to why the assertions of general utility in this application, given the suggested mechanism of action. As such, the Examiner has failed to meet the burden discussed in *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971), where it is noted that:

> a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond to those used in describing and defining the subject matter sought to be patents *must* be taken as in compliance with the enabling requirement of the first paragraph of § 112, *unless* there is a reason to doubt the objective truth of the statements contained therein, which must be relied upon for an enabling disclosure.

An over thirty-year-old case, discussing the state of the art at that time, is not a reason to doubt the truth of the asserted utility here.

Turning now to the contents of the evidence of record, Applicants have submitted copies of published papers showing that a monomeric ansamycin compound, 17-allylamino-geldanamycin (17-AAG), which is mentioned in the specification on Page 8, line 15 and other hsp90 inhibitors are efficacious in a variety of tumor types including breast cancer, ovarian cancer, pancreatic cancer and gastric cancer (the cancer types specifically mentioned on Page 8, lines 9-11 of the application), other HER kinase overexpressing tumors, and tumors which do not over express HER kinase. For example, Yang et al. (Exhibit A), report inhibition of glioma (brain tumor) cells with 17-AAG. Okabe et al. (Exhibit B) reports *in vivo* activity of herbimycin A (an ansamycin antibiotic) against leukemia cells. Kelland *et al* (Exhibit C, JNCI 91: 1940, 1999) achieved tumor cytostasis in two human colorectal carcinomas, HT29 and BE for the July 7, 2005 duration of drug treatment with 17-AAG. Burger *et al* (Exhibit D Proc. AACR, 41: Abstract # 2844, 2000) reported potent effects of 17-AAG against a melanoma xenograft and, interestingly, preliminary data from the London arm of the 17-AAG trial indicates that melanoma (2/6 objective responses) may be a responsive tumor (Exhibit E Banerji *et al*, Proc. ASCO, Abstract # 326, 2001) 17-AAG has also been used in studies with prostate cancers, and it has been shown that this administration resulted in dose-dependent inhibition of androgen-dependent and -independent prostate cancer xenografts. (Exhibit F Solit et al., *Clin. Cancer Res.* 8: 986-993, 2002). 17-AAG has also been shown to enhance paclitaxel-mediated cytotoxicity in lung cancer cells (Exhibit G Nguyen et al, *Ann. Thorac. Surg.* 72: 371-379, 2001); and to modulate metastasis phenotypes in non-small cell lung cancer (Exhibit H Nguyen et al., *Ann. Thorac. Surg.*

70: 1853-60, 2000). Thus, the efficacy of compounds that bind to the hsp90 receptor span a wide range of unrelated cancers, thereby refuting the Examiner's statement that generalized cancer therapy is inherently unbelievable.

As observed in *In re Bowen*, 492 F. 2d 859, 181 U.S.P.Q. 48 (C.C.P.A. 1974) reasons are required to support an enablement rejection where the operability of materials beyond the scope of specific examples is challenged by the Examiner. The Examiner has provided no such reasoning here. The evidence of record shows that monomeric compositions have utility against a broad range of cancers. The Examiner does not contest this. He argues, however, that the evidence is not relevant because it not directed to the dimeric compositions of the invention. In making this argument, however, the Examiner has not provided a single reason why a person skilled in the art, would doubt that the dimers would have the same range of effectiveness and utility as the monomers. Thus, he has failed to provide an objective reason to doubt the statements of utility in the specification as required by *In re Marzocchi.*

The Examiner rejected the previously pending claims under 35 USC § 112, second paragraph. Applicants note that this rejection contains paragraphs numbered (i) and (iii) but not (ii). Thus, it is unclear if something is missing. This was pointed out to the Examiner in a telephone interview, but the Official Action was not modified.

The Examiner states that the claims are indefinite because of the term "linker" because "one skilled in the art cannot say which 'linker' is intended." Plainly this rejection cannot apply to all of the previously pending claims, or to the currently pending claims in which the nature of the linker is specified. The Examiner is requested to specifically identify what claims this argument applies to. Further, the Examiner is applying an incorrect standard. Definiteness requires that a person skilled in the art be able to understand what falls within the scope of the claim, not recite everything that might fall within the scope of the claims. The person skilled in the art. looking at a particular compound, could clearly tell if there was something, i.e. a linker, between the two binding moieties. This being the case, there is no lack of definiteness or clarity.

The Examiner also states that the term "bind" is indefinite because it is a process that "cannot be observed, merely inferred, which is unreliable." Applicants respectfully submit that the term "bind" is used routinely in the relevant art to refer to the interaction between two molecules, hence the reference to "binding sites," and that the inferential use of competitive binding assays is also standard practice. The Examiner has not indicated why a person skilled in the relevant art would have any doubt as to the meaning of the tem. The Examiner has not stated why or provided any evidence to support the argument that inference is "unreliable." Applicants also submit that the location at which ansamycin antibiotics bind is known in the art, and indeed directly observed. (See Stebbins et al. of record). Thus, the Examiner has failed to establish that the claim is indefinite because of the use of the term "bind."

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Applicants further note that the Examiner states in this paragraph iii that "the metes and bounds of 'ansamycin antibiotic' are not known" but has not repeated this rejection as a separate ground for lack of definiteness. Applicants have fully responded to this argument previously, and the Examiner may not simply ignore the evidence of routine use and understanding in the art without establishing his own credentials by way of declaration and the reasons which entitle him to state that all uses in the art, including prior a\patents, are somehow wrong.

The Examiner further mentions that Hsp90 is a family of proteins, and that the pockets are not all the same. Applicants submit that the binding pockets in these proteins are highly conserved, and that the binding behavior is comparable . If the Examiner wishes to argue differently, then he has the obligation to present evidence to support his position. *In re Ahlert*, 165 USPQ 418, 420-21 (CCPA 1970)

The Examiner also provisionally rejected the claims for obviousness-type double patenting over Application Serial No. 09/937,192 which is presently on appeal. Applicants will address this rejection through the filing of a terminal disclaimer, if appropriate, when an indication of allowable claims is received

For these reasons, this application is now considered to be in condition for allowance and such action is earnestly solicited.

Respectfully submitted,

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